

Notice of Allowability

Application No.

09/695,769

Examiner

Joanne Hama, Ph.D.

Applicant(s)

PROCKOP ET AL.

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 10/18/07.
2. ☒ The allowed claim(s) is/are 1-12, 14-19, 21-26 and 31-35.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☐ All b) ☐ Some* c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
 5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
 - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date _____
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 18, 2007 has been entered.

Claims 13, 20, 27-30, 37-41 are cancelled. Claims 1, 24, 31, 32 are amended.

Claims 1-12, 14-19, 21-26, 31-36 are under consideration.

Withdrawn Rejections

35 U.S.C. § 112, 1st parag., New Matter

Applicant's arguments, see pages 9-12 of Applicant's response, filed October 18, 2007, with respect to the rejection of claims 1-12, 14-19, 21-26, 31-36 have been fully considered and are persuasive. Applicant has amended the claim to remove the phrase, "results in a greater total number of cells to be obtained compared to the total number of cells" and inserted the phrase, "enhanced expandability" to describe the effect observed in the claimed method. The rejection of claims 1-12, 14-19, 21-26, 31-36 has been withdrawn.

35 U.S.C. § 112, 1st parag., Enablement

Applicant's arguments, see pages 12-14 of Applicant's response, filed October 18, 2007, with respect to the rejection of claims 1-12, 14-19, 21-26, 31-36 have been fully considered and are persuasive. Applicant has amended the claim to remove the phrase, "results in a greater total number of cells to be obtained compared to the total number of cells" and inserted the phrase,

“enhanced expandability” to describe the effect observed in the claimed method. The rejection of claims 1-12, 14-19, 21-26, 31-36 has been withdrawn.

35 U.S.C. § 112, 2nd parag.

With regard to the cells being plated at "50 cells per square centimeter of growth factor," as recited in claims 1, 24, 32, the rejection is withdrawn, as the claims have been amended to recite, "50 cells per square centimeter of growth surface," by Applicant and the below Examiner's amendment. As such, the rejection as it applies to this issue is withdrawn. The rejection of claims 2-12, 14-19, 21-22, 25-26, 33-36, as they depend on claims 1, 24, 32 is withdrawn.

With regard to the rejection of claim 24, lines 8-9, for lacking antecedent basis for reciting the phrase, "the proliferated isolated marrow stromal cells," Applicant has amended the claim to indicate that the "isolated human marrow stromal cells proliferate." Indicating that the proliferated isolated marrow stromal cells refer to those that are isolated overcomes the rejection. The rejection of claim 24 is withdrawn.

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Dr. Carol Laherty on December 19, 2007.

The application has been amended as follows:

1. Claim 1 has been amended as follows:

A method of inducing proliferation of isolated human marrow stromal cells in vitro by plating and replating said cells at an initial density of 50 cells or less per square centimeter of growth surface wherein the method generates enhanced expandability of marrow stromal cells relative to results in a greater total number of cells to be obtained compared to the total number of cells obtained from plating and replating at an initial density of more than 50 cells per square centimeter of growth surface, the method comprising:

(1) providing the isolated human marrow stromal cells and a growth medium comprising a mammalian serum to a growth surface such that the initial density of the isolated human marrow stromal cells is 50 cells or less per square centimeter of growth surface,

(2) incubating the growth surface of step (1) under growth-promoting conditions, whereby the human marrow stromal cells proliferate, and

(3) replating the proliferated marrow stromal cells and a growth medium comprising a mammalian serum to a second growth surface at least one time such that the initial density of the replated isolated human marrow stromal cells is 50 cells or less per square centimeter of growth surface, wherein the replating allows the cells to expand by a factor of at least 10-fold.

2. In claim 2, line 2, the phrase, "less than about 25 cells" was deleted and the phrase, "25 cells or less" was inserted.

3. In claim 3, line 2, the phrase, "less than about 12 cells" was deleted and the phrase, "12 cells or less" was inserted.

4. In claim 4, line 2, the phrase, "less than about 10 cells" was deleted and the phrase, "10 cells or less" was inserted.

5. In claim 5, line 2, the phrase, "less than about 6 cells" was deleted and the phrase, "6 cells or less" was inserted.

6. In claim 6, line 2, the phrase, "less than about 3 cells" was deleted and the phrase, "3 cells or less" was inserted.

7. In claim 7, line 2, the phrase, "less than about 1.5 cells" was deleted and the phrase, "1.5 cells or less" was inserted.

8. In claim 8, line 2, the phrase, "less than about 1.0 cells" was deleted and the phrase, "1.0 cell or less" was inserted.

9. In claim 9, line 2, the phrase, "less than about 0.5 cells" was deleted and the phrase, "0.5 cells or less" was inserted.

10. In claim 10, line 3, the word, "about" was deleted.

11. In claim 11, line 3, the word, "about" was deleted.

12. In claim 14, line 3, the word, "about" was deleted.

13. In claim 15, line 3, the word, "about" was deleted.

14. In claim 16, line 4, the phrase, "less than about 50 cells" was deleted and the phrase, "50 cells or less" was inserted.

15. In claim 17, line 3, the word, "about" was deleted.

16. In claim 18, line 2, the word, "about" was deleted.

17. Claim 24 has been rewritten as follows:

A method of enhancing in vitro proliferation of isolated human marrow stromal cells growing on a surface in the presence of a growth medium comprising a mammalian serum by plating said cells at an initial density of 50 cells or less per square centimeter of growth surface, the method comprising supplementing the growth medium with a conditioned medium, wherein the conditioned medium is obtained from a culture of producer human marrow stromal cells which are grown on a second surface at an initial density of at least 0.5 cells per square centimeter and which are incubated for at least 3 days, whereby the isolated human marrow stromal cells proliferate, and further wherein the proliferated isolated marrow stromal cells and a growth medium comprising a mammalian serum are replated at least one time to a third growth surface such that the initial density of the replated isolated human marrow stromal cells is 50 cells or less per square centimeter of growth surface, wherein the replating allows the cells to expand by a factor of at least 10-fold, wherein the method generates enhanced expandability of marrow stromal cells relative to plating and replating at an initial density of more than 50 cells per square centimeter of growth surface.

18. In claim 25, line 2, the word, "about" was deleted.

19. In claim 26, line 2, the word, "about" was deleted.

20. Claim 31 has been rewritten as follows:

A method of inducing proliferation of human marrow stromal cells in vitro by plating said cells at an initial density of 50 cells or less per square centimeter of growth surface, the method comprising isolating mononuclear cells from a bone marrow sample, incubating the mononuclear cells to yield colonies, isolating an individual colony, and incubating human

marrow stromal cells obtained from the isolated colony in a container having a growth surface, the container containing a growth medium comprising a mammalian serum and the cells at a density of 50 cells or less per square centimeter of growth surface, whereby the cells proliferate, and further wherein the proliferated isolated marrow stromal cells and a growth medium comprising a mammalian serum are replated at least one time to a second growth surface such that the initial density of the replated isolated human marrow stromal cells is 50 cells or less per square centimeter of growth surface, wherein the replating allows the cells to expand by a factor of at least 10-fold, wherein the method generates enhanced expandability of marrow stromal cells relative to plating and replating at an initial density of more than 50 cells per square centimeter of growth surface.

21. Claim 32 has been amended as follows:

A method of assessing the expandability of isolated human marrow stromal cells in vitro by plating said cells at an initial density of 50 cells or less per square centimeter of growth surface, the method comprising incubating isolated human marrow stromal cells on a surface in the presence of a growth medium comprising a mammalian serum at an initial density of 50 cells or less per square centimeter of surface and assessing the colony forming efficiency of the human marrow stromal cells, whereby the expandability of the human marrow stromal cells is approximately proportional to the colony-forming efficiency of the human marrow stromal cells, and further wherein the expanded isolated marrow stromal cells and a growth medium comprising a mammalian serum are replated at least one time to a second growth surface such that the initial density of the replated isolated human marrow stromal cells is 50 cells or less per square centimeter of growth surface, wherein replating allows the cells to expand by a factor of

at least 10-fold, wherein the method generates enhanced expandability of marrow stromal cells relative to plating and replating at an initial density of more than 50 cells per square centimeter of growth surface.

22. In claim 33, line 2, the word, "about" was deleted.

23. Claim 36 was cancelled.

The following is an examiner's statement of reasons for allowance:

It is noted that the 103 of record, Huang et al., 1997, Biotechnology Letters, 18: 89-92, is similar to that of the claimed invention, except Huang et al. use a different species of cells, mouse, and did not report observing enhanced expandability. Given that neither the art nor specification provide guidance that mouse would necessarily behave like the claimed human cells, the 103 rejection was not applied.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is (571) 272-2911. The examiner can normally be reached on Monday-Friday 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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JH

/Anne Marie S. Weh  /
Primary Examiner, A.U. 1633